



#### REMARKS

First, applicants would like to thank Examiners Venkat and Silverman for the in-person interview of November 29, 2005. In this interview, new claims 18-65 were discussed, as well as how the new claims are novel and unobvious over the prior art.

The Official Action states at page 2 that "claims 1-11 are pending in this action". However, applicant respectfully points out to the Examiner that claims 1-10 and 12-17 were pending as of the mailing date of this Official Action, per applicants' Preliminary Amendment filed August 19, 2004. In that Preliminary Amendment, claim 11 was canceled without prejudice to or disclaimer of the subject matter contained therein and claims 12-17 were added.

Upon entry of the amendments submitted herewith, claims 18-65 will be pending in this application. Applicants respectfully submit that the new claims do not add any new matter within the meaning of 35 U.S.C. §132 to the application. In this regard, applicants have specifically referenced herein in Section 1 of this Response where basis for the new claims exists in the specification.

Upon entry of the amendment, 48 claims will be pending in the application, one of which is an independent claim (claim 18). Accordingly, applicants submit herewith a check in the amount of

\$1400 for the excess claim fee (of 28 dependent claims in excess of twenty @ \$50/claim).

### **1. Basis for Amendments Presented**

As stated above, applicants have entered new claims 18-65 with this response. Applicants outline herein where basis for the new claims exists in the specification.

Claim 18: Original claims 1, 6 and 7 and page 2, second paragraph

Claim 19: Original claim 1 and page 6, paragraph 4

Claim 20: Original claims 1, 6 and 7

Claim 21: Original claim 1, page 6, paragraph 4 and page 22

Claim 22-23: Original claim 1 and pages 7/8, bridging paragraph

Claim 24: Original claim 1 and page 7, second paragraph

Claim 25: Original claim 2 and pages 6/7, bridging paragraph

Claim 26: page 7, last paragraph

Claim 27: page 8, second paragraph

Claims 28-29: page 7, fourth paragraph

Claim 30: page 7, fifth paragraph

Claim 31: original claim 4

Claim 32 : page 8, paragraph 5

Claim 33: Example B

Claim 34: Example D

Claim 35: Example E

Claims 36-37 : Page 8, paragraph 8

Claim 38 : original claim 8

Claims 39-44 : page 9, fourth paragraph

Claim 45: pages 9/10, bridging paragraph

Claim 46: page 10, paragraph 4

Claim 47: original claim 9

Claim 48: page 10, last paragraph

Claim 49: original claim 10

Claim 50: page 8, second last paragraph

Claims 51-52: page 8, paragraph 7

Claims 53-54: page 9, second paragraph

Claims 55-57: page 9, third paragraph

Claims 58-60: pages 21/22

Claims 61-62: Original claim 1 and page 6, paragraph 4

Claims 63-64: Original claim 2 and pages 6/7, bridging paragraph

Claim 65: page 9, fourth paragraph

Accordingly, applicants respectfully request that the Examiner enter all of the above amendments.

## **2. Priority Documents**

The Official Action does not acknowledge applicants' claim to priority.

It is respectfully noted that applicant filed this application under 35 U.S.C. §371 and the Notice of Acceptance of Application mailed March 30, 2005 indicates that "Priority Documents filed on August 19, 2004" were received. Applicants filed the PCT/IB/304 document issued by the International Bureau with this application on August 19, 2004 and have claimed a priority date of February 20, 2002.

Accordingly, applicant respectfully requests that the Examiner properly acknowledge applicants' claim to priority in the next communication.

**3. Rejection of claim 11 under 35 U.S.C. §112, 1<sup>st</sup> and**  
**2<sup>nd</sup> paragraphs**

The Official Action states that claim 11 is rejected under 35 U.S.C. §112, 1<sup>st</sup> and 2<sup>nd</sup> paragraph. In particular, the Official Action states, in relevant part:

Claim 11 recites 'prophylaxis of ... a disease... preventable by PDE4 inhibitors'. However, the claim does not specify, and the specification provides no guidance, as to what types of diseases are thus preventable. The specification speaks only to diseases that are treatable by PDE 4 inhibitors. Treatment and prevention are not the same.

The claim recites 'prophylaxis...of a disease...preventable by PDE 4 inhibitors.' However, the disclosure provides no guidance as to what types of diseases may be preventable by administration of such compounds. Thus, the claim is merely an invitation for a person of ordinary skill in the art to experiment to determine what diseases could be

prevented by the practice of the claimed method."

As stated above, applicants respectfully point out to the Examiner that claim 11 was canceled without prejudice to or disclaimer of the subject matter contained therein in the Preliminary Amendment filed August 19, 2004, rendering the basis of this rejection moot.

However, applicants have introduced new method claims 58-60, which do not contain the rejected "prevention" or "prophylaxis" language.

Accordingly, applicants respectfully request that the Examiner withdraw this rejection.

#### **4. Rejection of Claims 1-11 under 35 U.S.C. §103(a)**

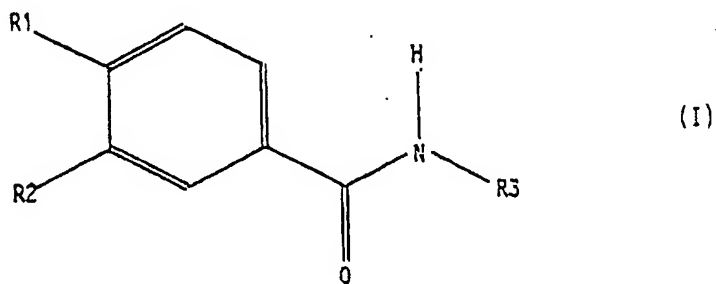
The Official Action states that claims 1-11 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Rennard, et al. (US Published Application No. 20030018071) in combination with Ghebre-Sellassie et al. (US Patent No. 6,667,362)

#### **RESPONSE**

Applicants respectfully point out to the Examiner that claims 1-11 have been canceled without prejudice to or disclaimer of the subject matter contained therein, rendering the basis for the rejection of these claims moot.

However, applicants have introduced new claims 18-65 which are somewhat similar to the rejected claims. In particular, for purposes of this Response, applicants will focus on new independent claim 18, which is an amended version of previously pending claims 1, 6 and 7, with the additional limitation that it is an immediate release dosage form. Upon entry of the amendment, claim 18 will be the only independent claim pending in this application.

Applicants note that claim 18 is drawn to a solid dosage form in tablet or pellet form for oral administration of a PDE 4 inhibitor, comprising a PDE 4 inhibitor together with polyvinylpyrrolidone as binder, and one or more other suitable pharmaceutical excipients, wherein the PDE 4 inhibitor is a compound of the formula I



in which

- R1 is difluoromethoxy,
- R2 is cyclopropylmethoxy and
- R3 is 3,5-dichloropyrid-4-yl,

or a salt of this compound, an N-oxide of the pyridine of this compound or a salt thereof,  
wherein said dosage form has immediate release of the PDE 4 inhibitor.

As was discussed in the in-person interview, the scope of claim 18 is not rendered obvious by the cited Rennard et al. and Ghebre-Sellassie et al. references because there is no motivation to combine the teachings of Rennard and Gebre-Sellassie et al.

The Examiner states in the Official Action that

it would be prima facie obvious...at the time of the invention to use poly(vinylpyrrolidone) in the composition Rennard, the result being the invention of the instant claims. The motivation for combining is provided by Ghebre, who teaches that formulations of drugs that are slightly soluble (such as roflumilast) which include poly(vinylpyrrolidone) offer increased bioavailability of the drug.

Applicants respectfully disagree. The primary Rennard et al. reference does not even discuss solubility of drugs. Further, Rennard et al. do not recognize the need for an immediate release dosage form containing polyvinylpyrrolidone (PVP) because it already teaches an "immediate release" tablet in Example 4 at Table 2.

Thus, a person of ordinary skill would not be motivated, upon reading Rennard et al., to combine it with the teachings of another reference to obtain an "immediate release" tablet of a slightly soluble drug.

Further, applicants point to the data in the specification at page 20 and in Figure 1. The data shows that the instantly claimed dosage forms comprising roflumilast and PVP lead to higher serum levels of roflumilast in the blood more quickly than the dosage forms comprising roflumilast and no PVP.

Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness against the presently pending claims. Further, if the Examiner insists on maintaining that he has established a *prima facie* case of obviousness against the presently pending claims, the data presented in the specification clearly demonstrates unexpected results which would rebut this alleged *prima facie* case.

As such, applicants respectfully request that the Examiner reconsider and withdraw the rejection.

**CONCLUSION**

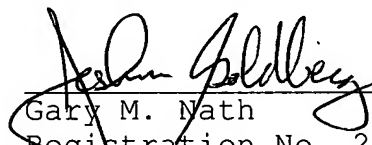
In view of the foregoing, applicants respectfully request the Examiner to reconsider and withdraw the rejection of the claims and to allow pending claims 18-65.

If the Examiner has any questions or wishes to discuss this matter, the Examiner is welcomed to telephone the undersigned attorney.

Respectfully submitted,

**NATH & ASSOCIATES PLLC**

Date: December 1, 2005

  
\_\_\_\_\_  
Gary M. Nath  
Registration No. 26,965  
Joshua B. Goldberg  
Registration No. 44,126  
Sheldon M. McGee  
Registration No. 50,454  
Customer No. 34375

**NATH & ASSOCIATES PLLC**

1030 15th Street N.W., 6th Floor  
Washington, D.C. 20006-1203  
Tel: (202) 775-8383  
Fax: (202) 775-8396  
JBG/SMM\ROA